

## REMARKS

This Amendment is submitted in response to the Office Action mailed on February 19, 2010. No fee is due in connection with the Amendment. The Commissioner is hereby authorized to charge any fees that may be required or credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 3712036-746 on the account statement..

Claims 1-4, 8-9, 11-16, 22-23 and 25 are pending in this application. Claims 5-7, 10, 24 and 26 were previously canceled without prejudice or disclaimer, and Claims 17-21 were previously withdrawn. In the Office Action, Claims 1-4, 9 and 15 are rejected under 35 U.S.C. §102. Claims 1-4, 8-9, 11-16, 22-23 and 25 are rejected under 35 U.S.C. §103. In response, Claims 1, 9, 15 and 22 have been amended, and Claim 3 has been canceled. The amendments do not add new matter. In view of the amendments and/or for at least the reasons set forth below, Applicants respectfully submit that the rejections should be reconsidered and withdrawn.

In the Office Action, Claims 1-4, 9 and 15 are rejected under 35 U.S.C. §102(b) as being anticipated by cis-trans Lycopene Isomers, Carotenoids, and Retinol in the Human Prostate by Clinton et al. ("*Clinton*"). In contrast, Applicants respectfully traverse the rejection for at least the reasons set forth below.

Applicants note that the Office Action cites *Clinton* in the initial anticipation rejection, but then refers to the Journal of Food Science, Vol. 52, No. 3, pp. 669-72 (1987) by Chandler et al. ("*Chandler*") for the main argument. Applicants will presume that *Chandler* is the actual cited reference for the anticipation rejection instead of *Clinton*.

Currently amended independent Claims 1, 9 and 15 recite, in part, a composition comprising at least one carotenoid-containing material, enriched in *cis*-isomer of the carotenoid compound, wherein the carotenoid-containing material is in a form selected from the group consisting of an extract, a concentrate, an oleoresin and combinations thereof. Independent Claim 22 recites, in part, a method for improving skin health comprising the step of administering to a patient in need of improved skin health at least one carotenoid-containing material, enriched in *cis*-isomer of the carotenoid compound, wherein the carotenoid-containing material is in a form selected from the group consisting of an extract, a concentrate, an oleoresin and combinations thereof. The amendments are supported in the specification, for example, at

U.S. Patent Publication No. 2007/0098820, paragraphs 21-22 and 24. The carotenoid compound is selected from the group consisting of lycopene, zeaxanthine, beta-cryptoxanthin, capsanthine, canthaxanthine, phytofluene, phytoene, and combinations thereof, and the *cis:trans* isomer ratio of the carotenoid compound is from 30:70 to 90:10.

Carotenoids are natural products that have beneficial effects such as alleviating chronic diseases. Isolated or enriched carotenoid compounds extracted from a natural source such as a plant or an animal are already known in the art. However, the carotenoids in these naturally-occurring compounds are insufficiently bioavailable and, thus, their full beneficial effects cannot be realized. In contrast, the present claims provide a carotenoid compound with improved bioavailability. The *cis*-isomer content of naturally-occurring carotenoid compounds that are extracted from plants or animals is low. For this reason, after the naturally-occurring carotenoid compounds are extracted from the plant or animal, they are subjected to further treatment such as microwave irradiation or solubilisation followed by phase separation in order to modify the isomer profile of the carotenoid. By subjecting the naturally-occurring carotenoid compound to additional treatment to increase its *cis*-isomer content such that the *cis:trans* isomer ratio is from 30:70 to 90:10, the bioavailability and/or bioefficacy of the carotenoid compound is increased.

In an embodiment, suitable plant or vegetable concentrates are obtainable by drying or freeze-drying the fresh-cut plants or vegetables or the respective roots, fruits or seeds thereof and then optionally grinding or granulating the dried material. Plant or vegetable extracts can be obtainable by extracting the fresh-cut or processed plants or vegetables or the respective roots, fruits or seeds thereof for example with water or with one or more food grade solvents or with a mixture of water and one or more food grade solvents. Preferably, the extracts and concentrates according to the present claims may be lipidic or aqueous. Because carotenoids are liposoluble, extraction with water will remove unwanted constituents that are water-soluble such as sugars, amino acids, soluble proteins, organic acids, for example.

In another embodiment, the carotenoid-containing material is an oleoresin. For example, oleoresins are obtained by lipidic extraction using a solvent compatible with the food business, cosmetics or pharmaceuticals. Oleoresins prepared by conventional methods have a content in carotenoid of about 0.05% to 50% by weight. Their content of all-trans isomer of carotenoids is usually higher than that of *cis* isomers, e.g. the ratio of *cis-trans* isomers of lycopene in a selected tomato oleoresin is about 7:93. Oleoresins are preferred starting material for obtaining the

primary composition according to the present invention, because they contain other carotenoids or antioxidants such as Vitamin E, which also stabilize the composition. The activity and stability of the carotenoid compound in the oleoresin is improved, in particular during the isomerisation process and the yield of the cis-lycopene in the primary composition is also increased.

The carotenoid-containing material that is in the form of an extract, a concentrate or an oleoresin can be subjected to a microwave irradiation or to other treatments including non-thermal treatments. Conditions of the microwave irradiation depend on the quantity and quality of the material. If an oleoresin is used, the power and time are adjusted so that the temperature of the microwave oven is of at least 100 °C, preferably from 100 to 180 °C and most preferably from 115 to 140 °C. If an aqueous extract is used, a medium adapted to microwave irradiation may be used. The aim of the medium is to solubilize or disperse carotenoids. The losses can be minimised when the isomerisation is performed under nitrogen in the presence of antioxidants and in the absence of light. The isomerisation yield may also be improved by adding exogenous lipids in the medium.

The isomers of carotenoid-containing compound generated thereof may be subjected to a further treatment intended to modify the isomer profile of the primary composition according to the intended use. The enrichment in some specific cis-isomers can be achieved by solubilisation of cis-isomers in selected organic solvents followed by phase separation using centrifugation or filtration, for example. The cis:trans isomer ratio in the final primary composition can then be 30:70 to 90:10.

*Chandler* fails to disclose or suggest a number of elements of the present claims. *Chandler* fails to disclose or suggest a carotenoid-containing material in a form selected from the group consisting of an extract, a concentrate, an oleoresin and combinations thereof and having a *cis:trans* isomer ratio from 30:70 to 90:10 of a carotenoid compound as required by independent Claims 1, 9 and 15. *Chandler* also fails to disclose or suggest a carotenoid-containing material having a *cis:trans* isomer ratio from 30:70 to 90:10 of a carotenoid compound selected from the group consisting of lycopene, zeaxanthine, beta-cryptoxanthin, capsanthine, canthaxanthine, phytofluene, phytoene, and combinations thereof as required by independent Claims 1, 9 and 15.

The Patent Office asserts that *Chandler* discloses a canned tomato as being an extracted and concentrated tomato. Applicants respectfully submit that a canned tomato disclose by

*Chandler* is merely that, one or more tomatoes in a can. The tomato may be process in the form of being cooked or sterilized, but there is no evidence in *Chandler* that the canned tomato includes any tomato in the form of an extract, a concentrate or an oleoresin.

*Chandler* further discloses separation and identification of *cis*- and *trans*- isomers of alpha- and beta-carotene. See *Chandler*, Title (“HPLC Separation of *Cis-Trans* Carotene Isomers in Fresh and Processed Fruits and Vegetables”); Introduction, page 669, paragraphs 3-5. Furthermore, the tables relied on by the Patent Office merely show the percentage of *cis*- and *trans*-isomers of beta-carotene. See *Chandler*, Tables 1-2. Nowhere does *Chandler* disclose or suggest a carotenoid compound selected from the group consisting of lycopene, xeaxanthine, beta-cryptoxanthin, capsanthine, canthaxanthine, phytofluene, phytoene, and combinations thereof in which the *cis:trans* isomer ratio is from 30:70 to 90:10.

For at least the reasons discussed above, Applicants respectfully submit that independent Claims 1, 9 and 15, along with any of the claims that depend from Claims 1, 9 and 15, are novel, nonobvious and distinguishable from *Chandler*. Accordingly, Applicants respectfully request that the rejection of the pending claims under 35 U.S.C. §102 be reconsidered and withdrawn.

In the Office Action, Claims 1-4, 8-9, 11-16, 22-23 and 25 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,965,183 to Hartal et al. (“*Hartal*”) in view *Chandler*. Applicants respectfully traverse the rejection for at least the reasons set forth below.

*Hartal* and *Chandler* alone or in combination fail to disclose or suggest each and every element of the present claims. In addition, the skilled artisan would have no reason to combine *Hartal* and *Chandler* to arrive at the claimed invention.

*Hartal* and *Chandler* alone or in combination also fail to disclose or suggest a carotenoid-containing material having a *cis:trans* isomer ratio from 30:70 to 90:10 of a carotenoid compound selected from the group consisting of lycopene, xeaxanthine, beta-cryptoxanthin, capsanthine, canthaxanthine, phytofluene, phytoene, and combinations thereof as required by independent Claims 1, 9, 15 and 22. *Hartal* and *Chandler* alone or in combination fail to disclose or suggest a carotenoid-containing material in a form selected from the group consisting of an extract, a concentrate, an oleoresin and combinations thereof and having a *cis:trans* isomer ratio from 30:70 to 90:10 of a carotenoid compound as required by independent Claims 1, 9, 15 and 22. *Chandler* is deficient with respect to the present claims as previously discussed.

*Hartal* discloses providing stable lycopene compositions with a high staining power for use in food coloring. See *Hartal*, column 2, lines 17-40. Nowhere does *Hartal* disclose or suggest any carotenoid-containing material having a *cis:trans* isomer ratio from 30:70 to 90:10 of a carotenoid compound in a form such as a lipidic extract or an oleoresin or even enriching the *cis*-isomer content of the lycopene to increase its bioavailability. In fact, the Patent Office admits that *Hartal* fails to disclose any *cis:trans* isomer ratio of from 30:70 to 90:10 and the specific carotenoid compounds. See Office Action, page 1, lines 1-22.

The Patent Office nevertheless asserts that merely because lycopene is a type of carotenoid, one of ordinary skill in the art would reasonably expect that lycopene could be used as the type of carotenoid taught by *Chandler*. However, *Chandler* specifically states that the column used in its experiments “is highly selective toward carotene isomers and under the solvent conditions employed other carotene[oids] such as lycopene do not elute.” See *Chandler*, page 671, paragraph 2, lines 13-15. As such, one of ordinary skill in the art would not consider lycopene an obvious modification of carotene and would have no reason to use lycopene in the column of *Chandler* to analyze *cis-trans* isomer content.

Moreover, one of ordinary skill in the art understands that lycopene is distinct from carotene because *cis*-isomers of carotenoids only exist naturally for beta-carotene, not for lycopene. *Chandler* discloses that certain fresh fruits such as plums and nectarines have a *cis*-isomer content of beta-carotene greater than 20%. See *Chandler*, Table 2. In contrast, the *cis*-isomer content of lycopene for a tomato oleoresin is merely 7%. In order to increase the *cis*-isomer content of lycopene to greater than 20%, the oleoresin must be subjected to further treatment such as microwave irradiation or solubilisation followed by phase separation. Therefore, the *cis*-isomer content of carotene disclosed in *Chandler* is not necessarily the same for lycopene or any other carotenoid and, contrary to the Patent Office’s assertion, cannot be relied on for the disclosure of a *cis:trans* isomer ratio from 30:70 to 90:10 in the claimed carotenoid compounds.

Furthermore, one of ordinary skill in the art would have no reason to combine the cited references because *Chandler* teaches away from the present claims. In this regard, references must be considered as a whole and those portions teaching against or away from each other and/or the claimed invention must be considered. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve Inc.*, 796 F.2d 443 (Fed. Cir. 1986). “A prior art reference may be considered

to teach away when a person of ordinary skill, upon reading the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the Applicant.” *Monarch Knitting Machinery Corp. v. Fukuhara Industrial Trading Co., Ltd.*, 139 F.3d 1009 (Fed. Cir. 1998), quoting, *In re Gurley*, 27 F.3d 551 (Fed. Cir. 1994).

*Chandler* is entirely directed to determining the amount of *cis*- and *trans*- isomers of beta-carotene in certain food products to assess the vitamin A activity of the food products. See *Chandler*, page 669, Introduction, paragraphs 2-3 and 5. *Chandler* specifically teaches that “[i]somerization reactions of the all *trans* form to *cis*-isomers reduces the bioavailability of the carotenoids as vitamin A precursors.” See *Chandler*, page 669, paragraph 2, lines 4-6. *Chandler* further notes that the conversion of *trans* beta-carotene isomers to *cis*-isomers results in a 15 – 35 % loss of vitamin A value. See *Chandler*, page 669, paragraph 3, lines 2-5. Therefore, *Chandler* teaches away from increasing the *cis:trans* isomer content of a carotenoid to increase its bioavailability.

In contrast, the present claims are entirely directed to a compound enriched in *cis*-isomer of the carotenoid compound. In order to obtain a carotenoid compound with an increased *cis*-isomer content, a naturally occurring extract or oleoresin of carotenoid is subjected to further treatment intended to modify its isomer profile. By increasing the *cis:trans* isomer ratio up to from 30:70 to 90:10, the present claims provide a carotenoid compound with a higher bioavailability than the compound alone. This is in direct contrast to *Chandler*’s teaching that a higher *cis*-isomer content reduces the bioavailability of the carotenoid. Therefore, *Chandler* teaches away from compounds enriched in *cis*-isomer of the carotenoid compound in accordance with the present claims.

For at least the reasons discussed above, Applicants respectfully submit that independent Claims 1, 9, 15 and 22, along with any of the claims that depend from Claims 1, 9, 15 and 22, are novel, nonobvious and distinguishable from *Hartel* and *Chandler*. Accordingly, Applicants respectfully request that the rejection of the pending claims under 35 U.S.C. §103(a) be reconsidered and withdrawn.

For the foregoing reasons, Applicants respectfully request reconsideration of the above-identified patent application and earnestly solicit an early allowance of same. In the event there remains any impediment to allowance of the claims that could be clarified in a telephonic interview, the Examiner is respectfully requested to initiate such an interview with the undersigned.

Respectfully submitted,

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Date: May 5, 2010